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Application of robotic surgery in cytoreductive surgery for advanced ovarian cancer

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Abstract: *It has been a hot topic to correctly evaluate the effect of operation mode and operation approach on patient survival. The robotic surgery system has many advantages such as flexible, stable and delicate, which has excellent results in complex surgeries compared with laparoscopic surgery. The robotic surgery has been applied in the stage operation of early ovarian cancer, the debulking surgery of advanced ovarian cancer and the debulking surgery of recurrent ovarian cancer. This review summarizes the application and controversy of minimally invasive surgery in the treatment of advanced ovarian cancer, and focuses on the feasibility and safety of robotic systems.*

Keywords: *Robotic surgery; Cytoreductive surgery; Laparoscopy; Ovarian cancer*

1. Introduction

Ovarian cancer is a common gynaecological malignancy, with approximately 314,000 new cases and 207,000 deaths each year. It has an insidious onset and more than 70% of patients are already at an advanced stage by the time they are diagnosed, and are prone to chemotherapy resistance and recurrence.

The treatment of choice for advanced ovarian cancer is Primary Debulking Surgery (PDS) combined with post-operative chemotherapy. The goal of the procedure is to achieve satisfactory tumour reduction where possible, i.e. residual tumour diameter of ≤1cm or no visible tumour remaining (R0). Satisfactory tumour cell reduction is an important prognostic factor for patients with advanced ovarian cancer. However, as some patients are unable to achieve satisfactory tumour reduction at the time of initial assessment or are unable to tolerate major surgery, Neoadjuvant Chemotherapy (NACT) combined with Internal Debulking Surgery (IDS) is increasingly being used in clinical practice.

Open surgery is the most classic surgical approach for tumour reduction, with the advantages of adequate exposure of the surgical field and direct access to the lesion by the operator, but the shortcomings of large surgical incisions and perioperative complications lead to slow postoperative recovery. With the continuous development of minimally invasive technology, laparoscopy has been widely used in the field of gynaecology due to its advantages of less trauma, clear surgical field and less bleeding. As an advanced minimally invasive technique, the robotic surgical system consists of three parts: a surgeon's console, a simulated instrument hand and an image processing system. It makes full use of all the advantages of traditional laparoscopy, but also has the advantages of three-dimensional imaging, a more flexible robotic arm, tremor filtering and a short learning curve, which facilitates the operator's precise operation. Since 2005, when the US Food and Drug Administration (FDA) approved the use of robotic surgery systems for gynaecological surgery, their application in the field of gynaecological oncology has matured, and they have certain advantages in endometrial and cervical cancer surgery. The robotic surgical system has been approved by the FDA for use in gynaecological oncology. Robotic surgical systems are safe and feasible for fully staged surgery in early-stage ovarian cancer. However, its use in advanced ovarian cancer is controversial. This article summarises the application and progress of robotic surgical systems in advanced ovarian cancer and discusses their clinical value and prospects.

2. Advances in laparoscopic surgery in advanced ovarian cancer

The main applications of laparoscopic techniques in ovarian cancer are: 1) comprehensive staging surgery for early-stage ovarian cancer; 2) disease assessment and decision-making in advanced ovarian

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cancer; 3) secondary tumour reduction in recurrent ovarian cancer; and 4) tumour cell reduction in some patients with advanced ovarian cancer is also used, but is still controversial.

An important prerequisite for NACT is a definitive pathological or cytological diagnosis. Ascites aspiration or mass aspiration is commonly used clinically to make a definitive diagnosis, but is prone to problems such as cytological false negatives. Laparoscopy allows adequate aspiration of ascites and multi-point pelvic and abdominal biopsy to improve diagnostic accuracy. The magnification of the laparoscope allows the operator to locate the primary lesion, especially in the exploration of small lesions in the upper abdomen, liver and spleen, diaphragm and pelvic peritoneum, an advantage not available with caesarean exploration. In addition, the surgeon can take biopsies of suspected lesions or lymph nodes, allowing for more accurate clinical staging. Compared to open surgery, laparoscopy has the advantage of being less invasive and more accurate in the diagnosis and staging of advanced ovarian cancer.

Laparoscopy can assess the feasibility of satisfactory tumour reduction. Based on the findings of Fagotti's team, Petrillo [1] et al. went on to refine the Predictive Index Value (PIV) and concluded that satisfactory tumour reduction could not be accomplished when the PIV score was ≥10. In 2017 Rutten [2] et al. proposed that PDS was considered unable to achieve satisfactory tumour reduction when extensive intra-abdominal metastases, or extensive bowel involvement or unresectable diaphragmatic surface metastases were seen laparoscopically. This study suggests that diagnostic laparoscopy may prevent the occurrence of ineffective caesarean sections in patients with advanced ovarian cancer. Fagotti [3] et al. first used laparoscopy in the preoperative evaluation of IDS and concluded that satisfactory tumour reduction was difficult to achieve in IDS when the total score was greater than 4.

In advanced ovarian cancer, the scope and content of laparoscopic IDS after NACT is similar to that of staged surgery for early-stage ovarian cancer, with reduced surgical difficulty and risk. The use of laparoscopy for tumour cytoreduction has been investigated nationally and internationally. The use of laparoscopy for IDS has been found to have the advantage of improving perioperative outcomes, with similar postoperative complication rates, satisfactory tumour reduction rates and prognostic outcomes to open surgery. A retrospective study by Melamed[4] et al. and Pereira[5] et al. both found that the minimally invasive group had a shorter length of stay and similar readmission rates, risk of perioperative death and survival rates to those of caesarean surgery. The 2020 LANCE study[6] found that the minimally invasive IDS group had better surgical outcomes such as transfusion rates, length of stay and satisfactory tumour reduction rates than the open IDS group, and their 2-year progression free survival (PFS) and overall survival (OS) were prolonged compared to the open IDS group. The CILOVE study[7] concluded that laparoscopic IDS is safe and feasible for patients who respond well to chemotherapy. In 2020 Jochum [8] et al. performed a systematic analysis of 19 retrospective studies and found that when the proportion of satisfactory tumour reduction was high, the 3-year mortality rate was significantly lower in the laparoscopic group than in the open group, and further subgroup analysis suggested the oncologic safety of minimally invasive surgery for all stages of ovarian cancer. More recently, Zeng[9] et al. systematically evaluated the effectiveness and safety of minimally invasive surgery versus open surgery for the treatment of advanced ovarian cancer after NACT, showing that the minimally invasive group had a significantly shorter hospital stay, with no significant differences in satisfactory tumour reduction rates and postoperative complications compared with the open group. OS was similar in the minimally invasive and open groups, but PFS was significantly higher in the minimally invasive group than in the caesarean group.

There are relatively few studies on the use of laparoscopic techniques for PDS, with some studies noted significant advantages of laparoscopic PDS compared to open surgery in terms of operative risk, postoperative recovery, perioperative complications, and similar survival outcomes. Ceccaroni[10] et al. rigorously selected 21 patients with advanced ovarian cancer for laparoscopic PDS and found a high rate of satisfactory tumour reduction, few perioperative complications and short chemotherapy intervals in this group, with no significant difference in prognosis compared with the open group.In 2021 Hou Zheng[11] et al. concluded that laparoscopic primary tumour cytoreduction in carefully selected patients with advanced epithelial ovarian cancer is feasible and safe, and its prognosis is not worse than that of open surgery.

Laparoscopic tumour cell reduction is safe and effective for selected patients with advanced ovarian cancer. However, there are still controversies surrounding the laparoscopic treatment of advanced ovarian cancer, such as tumour metastasis at the puncture site and tumour rupture. The patient's condition and quality should be fully assessed before surgery, and the operator's experience should be combined to select the appropriate surgical approach for patients with advanced ovarian cancer in order to maximise the benefits, rather than blindly choosing laparoscopic surgery.

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3. Robotic surgery in advanced ovarian cancer and its progress

Laparoscopic techniques are well developed and reflect certain advantages in tumour cytoreductive surgery. However, traditional laparoscopic surgery has limited operating space, long learning curve, poor visualization and operational stability, which limits its use in complex surgery. The advantages of the robotic surgical system, such as clear imaging, flexible operation and short learning curve, allow the operator to operate with precision and reduce damage in complex advanced ovarian cancer surgery.

Since Bandera and others have pioneered the use of robotic surgery in advanced ovarian cancer, more and more scholars have begun to investigate the safety and efficacy of robotic surgery in the treatment of advanced ovarian cancer. In 2010, Farghalay[12] et al. performed da Vinci robotic-assisted laparoscopic anterior pelvic contouring in a cohort of patients with advanced ovarian cancer, and the residual lesions were less than 1 cm. The surgical and near and long-term clinical results are acceptable and confirm the safety and feasibility of robotic surgery in tumour cytoreduction.

In 2013 Feuer[13] et al. investigated the feasibility and efficacy of robotic surgery for the treatment of advanced ovarian cancer and showed that compared with open surgery, robotic surgery required significantly longer operative time, but it resulted in less bleeding, shorter hospital stay, no significant differences in perioperative complications, postoperative lesion residual rates and 1-year survival, and also found that NACT was more common in the robotic group (52% vs 15%, $p = 0.0013$) , confirming that robotic surgery is safe and effective for ovarian cancer treatment. Existing studies investigated the role of NACT combined with IDS in the treatment of advanced ovarian cancer, concluding that NACT-IDS can reduce the complexity of surgery and the incidence of perioperative complications and provide patients with the opportunity for satisfactory tumour reduction, and that robotic-assisted laparoscopic IDS can take full advantage of the minimally invasive technique. Some studies found that robotic-assisted laparoscopic IDS has the advantages of reduced intraoperative bleeding, lower perioperative complication rates, shorter hospital stays, less postoperative pain and earlier postoperative feeding than open or conventional laparoscopic surgery. The advantages of robotic-assisted laparoscopic IDS include reduced intraoperative bleeding, reduced perioperative complications, shorter hospital stay, reduced postoperative pain, and early postoperative feeding.

Lymphatic metastases from ovarian malignancies are leapfrogging. NCCN Clinical Practice Guidelines state that tumour cytoreductive surgery should remove enlarged or suspicious lymph nodes where possible and that clinically negative lymph nodes do not need to be removed. Robotic-assisted laparoscopic resection of para-aortic lymph nodes is safe and has some advantages over open and laparoscopic surgery because of their high location and proximity to important blood vessels. Some studies found that the number of lymph nodes removed by open, laparoscopic and robotic approaches was similar, but one study robotic surgery was found to remove a greater number of para-aortic lymph nodes.

Complete excision of the lesion visible to the naked eye improves patient prognosis. Magrina [14] et al. found that survival outcomes in patients with advanced ovarian cancer were not influenced by the surgical approach, but rather correlated with surgical outcomes.In 2021 Zhang[15] et al. retrospectively studied 93 patients with advanced ovarian cancer undergoing IDS after NACT and found no significant differences in R0 rates, PFS and OS between the robotic and dissection groups, suggesting that the use of robotic surgery did not affect tumour reduction success or tumour survival indicators. This study also found that in patients undergoing robotic-assisted laparoscopic IDS, receiving more than six courses of preoperative chemotherapy was associated with reduced PFS and OS. In addition, one study found that robotic surgery applied to IDS prolonged patient survival [16] .

In 2021 Psomiadou[17] et al. performed a systematic review and found that in patients with advanced ovarian cancer after NACT, robotic-assisted laparoscopic IDS offers advantages in terms of operative time, bleeding, length of stay, postoperative complication rates and intermediate open rates, while ensuring that R0 is achieved. Patients who undergo robotic surgery demonstrate survival advantages over the open route. A recent meta-analysis comparing the perioperative and survival outcomes of robot-assisted laparoscopic surgery, conventional laparoscopic surgery and caesarean section for ovarian cancer showed that robotic and laparoscopic surgery resulted in shorter hospital stays, less bleeding, fewer complications and lower chances of transfusion compared to open surgery. There was no significant difference in 5-year overall survival between the three procedures.

Most of the available studies lack significant oncologic follow-up and the impact of robotic surgery on the prognosis of patients with advanced ovarian cancer is controversial. In addition, there are no clear criteria for the selection of advanced ovarian cancer cases suitable for treatment with robotic surgery.

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Magrina [14] et al. concluded that if patients with advanced ovarian cancer require liver, spleen or bowel resection, open surgery remains the treatment of choice. In 2022 Van Trappen et al. included 41 patients with advanced ovarian cancer without residual peritoneal lesions after NACT or without the need for complex surgical steps to assess perioperative and oncologic outcomes in the robotic and open surgery groups and showed that the body mass index (Body Mass Index, BMI) was significantly higher in the robotic surgery group than in the open group (27.8 kg/m2 vs 23.5 kg/m2, p=.006). This study confirms the oncologic safety of robotic surgery in advanced ovarian cancer and suggests that robotic surgery for tumor cytoreduction may be preferred in patients with advanced ovarian cancer who have responded well to neoadjuvant chemotherapy and do not have residual peritoneal disease, especially in combination with high BMI.

Currently, robotic surgical systems are mainly used for tumour cytoreduction after NACT for patients with advanced ovarian cancer. They circumvent the disadvantages of pure laparoscopic views and operations, improve anatomical accuracy and optimise surgical operations, and improve quality of life in the perioperative period for selected patients. Large-scale, multicentre, randomised controlled studies are still needed to evaluate the effectiveness of robotic surgery for advanced ovarian cancer, to further explore its relationship with prognosis and to define the criteria for appropriate patients.

4. Advantages and limitations of robotic surgery in advanced ovarian cancer

4.1. Advantages of robotic surgery applications

The magnified three-dimensional clear field of view of the robotic surgery system combined with the multidimensional flexible robotic arm that filters out tremors is very beneficial to the operator in completing fine pelvic operations, detecting microscopic lesions and precisely removing lesions in difficult areas in order to minimise patient trauma and speed up post-operative recovery. 3) The learning curve is shorter than that of conventional laparoscopy, facilitating the promotion of new techniques.4) The thick subcutaneous fat layer in obese patients makes it difficult to expose the surgical field, which may affect the surgical outcome and is associated with postoperative complications such as delayed incision healing and infection, and robotic surgery can be used in obese patients with advanced ovarian cancer to ensure the surgical outcome. The robotic surgery can be used in obese patients with advanced ovarian cancer to ensure the surgical outcome. 5) The da Vinci IV robot system simplifies the preoperative docking process and allows for more flexible arms than before, allowing multiple quadrant access to the abdomen without intraoperative re-docking, allowing the operator to rotate the instruments into the abdominal cavity to continue the procedure and complete bowel, liver and spleen and urology related procedures. 6) It relieves operator fatigue, enables remote consultation and technical guidance, facilitates multidisciplinary collaboration and frees up manpower.

4.2. Limitations of robotic surgical applications

The lack of tactile feedback may miss lesions in blind areas of the visual field such as between bowel collaterals and the diaphragm at the posterior margin of the liver, affecting the accuracy of lesion assessment after neoadjuvant chemotherapy and the operator's ability to perceive the tension of the thread and the tightness of the knot. Hand-assisted laparoscopic surgery, or the refinement of a better tactile feedback system in robotic surgery, offers ideas to address this. Adequate preoperative imaging assessment has an important role to play in reducing intraoperative lesion misses. 2) Port Site Metastasis (PSM) and tumour implantation, which is associated with multiple factors such as tumour aerosol, chimney effect and the establishment of a CO2 pneumoperitoneum. Studies Port Site Metastasis was not found to be an independent risk factor for overall survival, but its relationship with prognosis is unclear. The principle of tumour-free surgery, pneumoperitoneum evacuation before removal of the poke card, aspiration of intra-abdominal fluid and repeated flushing of the poke card may prevent metastases from the puncture site. 3) The high cost of surgery hinders the popularity of robotic surgery. In the future, improved health insurance policies and improved medical device manufacturing technology could make the cost more affordable for more patients. 4) The large size of robotic surgery systems and the complexity of docking procedures prolong surgery time. As the system is upgraded and the team works more closely together, the surgery can be performed more smoothly.

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5. Conclusion

Minimally invasive techniques have developed rapidly and the advent of robotic surgery has revolutionised surgery, with its high precision and flexibility ensuring the safety and effectiveness of surgery. The robotic surgical system for IDS after NACT for patients with advanced ovarian cancer has the advantages of significantly shorter hospital stay, reduced intraoperative bleeding, lower transfusion rate and risk of postoperative complications, and faster postoperative recovery, with survival rates similar to those of caesarean and laparoscopic surgery alone. Large sample sizes of randomised controlled trials are still needed to investigate the relationship between robotic surgical systems and the prognosis of patients with advanced ovarian cancer and to clarify the patient selection criteria for robotic surgery for IDS. With appropriate patient selection, the use of robotic-assisted laparoscopic tumour cytoreduction in advanced ovarian cancer will have a brighter future.

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